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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 08/444,790 | 05/19/1995 | MANFRED BROCKHAUS | 9189 | 5612 |

151 7590 07/12/2004
HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
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NUTLEY, NJ 07110

EXAMINER

MURPHY, JOSEPH F

ART UNIT PAPER NUMBER

1646

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/444,790

Applicant(s)

BROCKHAUS ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 62-99 is/are pending in the application.
- 4a) Of the above claim(s) 78-99 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 62-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 04262004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 62-99 are pending. Claims 78-99 stand withdrawn from consideration pursuant to 37 CFR 1.142(b).

Response to Amendment

The Office Action of 10/21/2003 set forth that newly submitted claims 78-99 are directed to an invention that is independent or distinct from the invention originally claimed. Applicant argues in the Reply filed 07/14/2004 that a constructive election occurs only when the applicant presents an amendment that results in independent or distinct groups of claims, which if examined together, would impose a serious burden on the Examiner without the election. However, the Office Action of 10/21/2003 set forth that the DNA of claims 78-99 and the receptor protein of claims 62-77 are independent and distinct, each from the other, because they are products which possess characteristic differences in structure and function, and each has an independent use, that is distinct for each invention which cannot be exchanged. In the instant case, nucleic acids and proteins are distinct because their structures and modes of action are different, which require non-coextensive searches, and furthermore, the DNA of claims 78-99 can be used as a hybridization probe, while the protein of claims 62-77 can be used for the production of antibodies or screening of compounds.

Applicant further argues that claims 78-99 and previously examined claims 69-77 commonly recite DNA sequences of Figure 1, and that in order to examine claims 69-77 the Examiner was required to conduct a thorough search of the prior art. However, the protein of claims 69-77 are classified in class 530, subclass 350, while the DNA of newly presented claims

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78-99 is classified in class 536, subclass 23.5. The separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search.

Applicant further argues that the Patent Office is required to formally issue a restriction requirement if it is alleged that distinct or independent inventions have been presented for prosecution. However, according to 37 CFR 1.145 if, after an office action on an application, the applicant presents claims directed to an invention distinct from and independent of the invention previously claimed, the applicant will be required to restrict the claims to the invention previously claimed if the amendment is entered. As was shown in the Office Action of 10/21/2003 the newly added claims are directed to an independent and distinct invention.

New issues, and remaining issues are set forth below.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 62-77 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to a homogenous protein which is found in nature, and as such is directed to non-statutory subject matter. This rejection could be obviated by directing the claims to an isolated homogeneous protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 62-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,981,701 (Wallach et al.), for reasons of record set forth in Paper No. 32, 4/17/2002, and 10/21/2003, and as evidenced by U.S. Patent No. 5,811,261 (Wallach et al.). U.S. Patent No. 5,981,701 has a priority date of 9/12/1988.

The rejection of record set forth that Wallach discloses purification of a tumor necrosis factor inhibitory protein, which interacts with TNF and inhibits the binding of TNF to its receptors and the cytotoxic effects of TNF (column 3 line 65 to column 4 line 4). The protein disclosed in Wallach has a molecular weight of 40-80 kD (column 16 line 44), and comprises an amino acid sequence that is identical to the sequence of the protein claimed in the instant application (column 16, line 56), thus claims 62-66, 69, 72, 75 are anticipated. Wallach further sets forth the methods to produce the TNF inhibitor protein recombinantly from host cells (column 12, line 11-column 15, line 53), thus anticipating claims 67-68, 70-71, 73-74, 76-77.

Applicant argues that facially, the rejection here is not based solely on Wallach I or on any other single prior art reference. The Patent Office has conceded, in fact, that Wallach I does not expressly disclose the claimed proteins. The Patent Office has attempted to fill that void with an "inherency" argument based upon the later-in-time Wallach 11, which contains disclosure

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significantly different from Wallach I and which is not prior art. However, a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to show that a characteristic not disclosed in the reference is inherent, see MPEP 2131.01, and Continental Can Co., in which the Federal Circuit wrote that an extra reference or evidence can be used to show an inherent characteristic of the thing taught by the primary reference: "To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Also note that the critical date of extrinsic evidence showing a universal fact need not antedate the filing date. See MPEP § 2124

Applicant further argues that the reliance by the Patent Office upon "claim 2" of Wallach I is also misplaced, because it is not a description of any polypeptide and is legally incapable of anticipating applicants' claims. However, claim 2 of Wallach I is directed to a protein which contains the 16 amino acid sequence as set forth in the claim, and the molecular weight of the protein claimed is the same as the size of the protein instantly claimed. Applicant argues that Wallach I, at best, describes a "substantially" purified fragment that is missing upstream and downstream amino acids, not the "homogeneous" protein having the different and complete sequence recited in the claims. However, the '701 patent does not claim the fragment of the protein, it claims the entire protein which comprises a fragment which has the 16 amino acid

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stretch as defined in the claims, and also sets forth the size of the complete protein, thus anticipating the claims of the instant application.

Applicant argues that claims 63-65 recite a "homogeneous" protein that "comprises the amino acid sequence of Figure 1 beginning at amino acid number 1 and ending approximately at amino acid number 180". As noted, Wallach I discloses only the 16 amino acid N-terminus" of its less-than-fully-purified protein and is absolutely silent as to the internal sequence and COOH-terminal end of the protein. However, the claims in the '170 patent are directed to a protein comprising the 16 amino acid sequence, and meet the length limitation, given the molecular weight set forth for the purified protein.

Applicant further argues that claims 69-77 recite a "homogeneous" protein that has the amino acid sequence "encoded by the DNA sequence of Figure 1 beginning at nucleotide number 121 and ending at approximately nucleotide number 627...." (Claim 69.). However, the claims are written using open language, i.e. they are directed to proteins which comprise the amino acids sequence 121-627 encoded by Figure 1, which includes the full length protein as set forth in the '701 patent. Furthermore, the limitation wherein the protein is recombinantly produced does not distinguish over the '701 patent because patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claims. *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985).

Applicant further argues that the open-ended language of "claim 2" of Wallach I is not a disclosure of any particular protein sequence. At most, claim 2 embraces any and all amino acid

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sequences - of any size - that may "contain" -- anywhere - the recited 16-mer fragment. As a matter of law, a claim of such sweeping scope cannot anticipate the particular structurally defined sequences recited in the claims here. However, Applicant's characterization of the claims in the '701 patent do not account for the functional limitations in the claim, which require the protein covered by the claims exhibit the functions of interacting with TNF and inhibiting its binding and cytotoxicity, thus the instant rejection is distinguishable for the case in In re Benno, because the claims contain both structural and additional functional language.

Applicant also argues that the Patent Office provided no evidence to support the assertion that the "protein" of Wallach I "inherently possess the sequence of SEQ ID NO: 2" of Wallach II, and that Wallach II describes different processes and different proteins than are described in Wallach I fairly and practically viewed. However, the rejection of record showed that the protein set forth in SEQ ID NO: 2 of the 261 patent comprises the 16 amino acid stretch as disclosed in the '701 patent, and the '261 patent discloses the tumor necrosis factor inhibitory protein interacts with TNF and inhibits the binding of TNF to its receptors and the cytotoxic effects of TNF (column 2 lines 1-3). The protein disclosed in the '261 patent has a molecular weight of 40-80 kD (column 9 lines 34-35), the same as disclosed in the '701 patent, and this serves as the evidentiary basis that the proteins are the same.

Applicant concludes that on this record, it is manifest that Wallach I does not identically describe the claimed polypeptide and that the rejection of claims 62-77 in view of Wallach I should be withdrawn. However, as set forth above, the proteins have an identical stretch of amino acids sequence, have the same size, and the same function, and are thus the same protein.

Claims 62-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,811,261 (Wallach et al.), for reasons of record set forth in paper No. 37, 8/21/2002, and 10/21/2003. U.S. patent No. 5,811,261 has a priority date of 09/12/1988 (the filing date of Application No. 07/243,092).

The rejection of record sets forth that the '261 patent discloses purification of a tumor necrosis factor inhibitory protein, which interacts with TNF and inhibits the binding of TNF to its receptors and the cytotoxic effects of TNF (column 2 lines 1-3). The protein disclosed in the '261 patent has a molecular weight of 40-80 kD (column 9 lines 34-35). the full amino acid sequence of the TNF inhibitory protein of Wallach is set forth in the '261 patent (see SEQ ID NO: 2). The sequence of SEQ ID NO: 2 of the '261 patent is 100% identical to the amino acid sequence of the protein claimed in the instant application, and is 100% identical from amino acids 1-180 of the protein claimed in the instant application. Thus, claims 62-66, 69, 72, 75 are anticipated. The methods to produce the TNF inhibitor protein recombinantly from host cells are disclosed in the Wallach patent (column 12, line 11-column 15, line 53), thus anticipating claims 67-68, 70-71, 73-74, 76-77.

Applicant argues that the Examiner cannot rely on the September 12, 1988 filing date of the '092 application in the present rejection because the subject matter relied upon in the rejection was not described or enabled in the '092 application. Applicant further argues that When a rejection relies on an issued U.S. patent claiming benefit to an earlier filed application as a continuation-in-pad, it is incumbent upon the Patent Office to make the necessary factual determinations as to whether the subject matter in the patent asserted is supported by the earlier filed application, i.e., complies with the requirements of 112, first paragraph, and where, as here,

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the rejection fails to make these factual determinations, the rejection is insufficient as a matter of law and must be withdrawn. However, tumor necrosis factor inhibitory protein was disclosed in the parent application 07/243,092, as well as the partial sequence, which demonstrates that this is the same protein as set forth in the '261 patent, with the amino acid sequence as set forth in SEQ ID NO: 2. The protein set forth in SEQ ID NO: 2 of the '261 patent comprises the 16 amino acid stretch as disclosed in the '701 patent, and the '261 patent discloses the tumor necrosis factor inhibitory protein interacts with TNF and inhibits the binding of TNF to its receptors and the cytotoxic effects of TNF (column 2 lines 1-3). The protein disclosed in the '261 patent has a molecular weight of 40-80 kD (column 9 lines 34-35), the same as disclosed in the '701 patent, and this serves as the evidentiary basis that the proteins are the same. The proteins have an identical stretch of amino acids sequence, have the same size, and the same function, and are thus the same protein.

Conclusion

No claim is allowed.

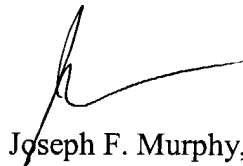
Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

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The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
July 8, 2004